



What has Covid-19 change in acute pancreatitis?

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Abstract. Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2), the virus that caused COVID-19, first emerged in Wuhan, China, in December 2019 and in March 2020 was declared a pandemic and a serious public health issue. While the SARS-CoV-2 can cause frequently fever, cough, and dyspnea, the gastrointestinal symptoms as diarrhea, abdominal pain, nausea, vomiting, dysgeusia are also encountered. The virus has an affinity for ACE2 receptors that are also encountered in pancreas. Pancreatic injury can appear especially in severe COVID-19. The mechanism is still unknown, but that are date that consider a direct and indirect mechanism.

KEY WORDS: SARS COV2 INFECTION, ACUTE PANCREATITIS,

SARS CoV2 INFECTION

Epidemiology

The coronavirus disease 2019 (COVID-19) pandemic has now affected >61 million people and caused >6.4 million deaths worldwide (1). In Romania 3.26 million people were affected and 66 thousand died from COVID-19 (2).

The first case of coronavirus infections was described in domesticated chickens in North America in the late 1920s (3). Human coronaviruses were discovered in the 1960s and presently seven strains cause disease (4). Four of this strains, Human coronavirus OC43 (HCoV-OC43), human coronavirus HKU1 (HCoV-HKU1), human coronavirus 229E (HCoV-229E) and human coronavirus NL63 (HCoV-NL63), cause mild disease. The severe acute respiratory syndrome coronavirus (SARS-CoV1), Middle East respiratory syndrome-related coronavirus (MERS-CoV) and severe acute respiratory syndrome coronavirus 2 (SARSCoV-2) may potentially cause severe disease (5). Outbreaks of SARS-CoV-1 and MERS-CoV infections occurred in 2002 and 2012, respectively (6). The most frequent symptoms are fever and respiratory symptoms. The gastrointestinal manifestation can also be present as a manifestation of SARS CoV2 infection (7).

In 11st march 2020, WHO declares SARS CoV2 pandemic that effect directly the society by it's manifestations, and indirectly by affecting the economies and producing a shift in power and mentality paradigms (8).

Transmission

The transmission of the SARS-CoV-2 occurs through human-to-human contact, either directly through respiratory droplets or indirectly by touching contaminated surfaces (9). In addition, it has also been discovered that SARSCoV-2 can remain airborne for up to 3 hours (9), increasing the risk of contracting the virus (9). The presence of SARS-CoV-2 RNA in urine and feces has been detected leading to the implication of the fecal-oral route in its transmission as well. Multiple studies have confirmed the presence of SARS-nCoV-2 RNA in the stool of COVID-19 patients, including

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some who never tested positive in the upper respiratory tract (10).

A large proportion of the new infections (25-50%) occur secondary to viral shedding by asymptomatic people. (the mean incubation period ~ 5 days, with a range 0-14 days). Viral shedding starts 1 to 2 days before the symptoms onset and is the highest in the early stages of the infection. Virus lingered in the serum 16 days, in the respiratory system 18 days and in stool from 22 days up to 10 weeks (11).

Clinical manifestation

While 80% of the patients have asymptomatic forms, in 20% of the patients the disease can be moderate 17% or severe 3%. COVID19 affects all ages from childhood to older adults older adult (12). The most common complaints are fever, cough, and dyspnea, and less frequently gastrointestinal symptoms like diarrhea (13). Less common symptoms include abdominal pain, nausea, vomiting, dysgeusia, and bloody diarrhea. Importantly, studies suggest that a fraction of COVID-19 patients experience digestive manifestations in the absence of respiratory symptoms or fever (13). Older age group (65 years or older) is at higher risk of developing severe SARS-CoV-2 infection because of higher proportion of established co-morbidities (respiratory, diabetes, obesity, hypertension) (12). The mortality can reach up to 1,5-3% (12).

ACUTE PANCREATITIS

Introduction

Acute pancreatitis (AP) can have numerous causes. The most frequent are alcohol and lithiasis. Viral pancreatitis is also a well known viral etiology. There are a number of viruses associated with etiology of acute pancreatitis: cytomegalovirus, Epstein Barr virus, hepatitis (A,B,C,D,E), primary HIV infection, Coxsackie, Herpes simplex, varicella Zoster, mumps, measles, adenovirus (14).

Starting from this observation, the researchers presumed that the pancreas can be also a potential coronavirus target (14).

Studies have shown that in SARS CoV2 infection the virus was not detected only in the lung, liver, kidney, gastrointestinal tract but in the pancreas as well (11).

Ethiopathology

SARS-CoV-2 enters host cells through ACE2 receptors. (15) ACE 2 receptors were identified in pancreas exocrine and islets. The density of ACE 2 receptors in pancreas is still controversial, but the studied have observed that there are pancreatic injury especially in severe COVID-19 (15).

The mechanism through SARS CoV 2 affects the pancreas it is still unknown. Some authors consider that the virus have a cithopathic effect mediated by local SARS CoV2. Another theory is that the pancreatic injury appear secondary to systemic inflammatory and imunocellular response (16).

A multiple-hit theory in AP has been recognized and multiple etiological factors can contribute to AP development (17). The direct effect of the virus is rare and frequently affecting immunocompromised patient (17,18). The ACE 2 receptors are expressed in the pancreas and pancreatic injury has been recognized in COVID-19 patients, especially in severe cases. In COVID-19, the thrombogenic state can also contribute to pancreatic hypoperfusion and ischemia. Another theory is that the medication which have been used for treatment of COVID-19 affect directly the pancreas and cause AP. Tocilizumab can induce hypertriglyceridemia and has been associated with the development of AP from 2 weeks of treatment onset (19). Another medication that increase serum triglyceride levels is propofol infusion in critically ill, secondary to the lipid emulsion vehicle, which can contribute to hypertriglyceridemia and pancreatic injury in COVID-19 patients(19). Lopinavir/ritonavir, can lead to lipid metabolism abnormalities in COVID-19 patients(20), and clinicians should be aware of possible treatment side-effects, although there were no cases of AP described. In some cases, the clinicians use doxycycline, lisinopril, estrogens and steroids which are associated with AP development (20).

Diagnosis

The diagnosis of AP, based on the modified Atlanta criteria, requires two of the following three features: typical abdominal pain, serum lipase activity (or amylase activity) at least three times greater than the upper limit of normal, and characteristic findings of AP on contrast-enhanced computed tomography (CECT) and less commonly magnetic resonance imaging or transabdominal ultrasonography (21).

The timing of pancreatic injury is still controversial. In a recent study, Wang et al. described that the AP appear in the same time with the SARS CoV2 pneumonia (22). In another case report, Ellhence et al. reported that the diagnosis of SARS CoV 2 infection was made several days after admission for AP. The patient developed respiratory failure as a complication of severe AP and was tested positive for COVID-19 several days (39-91 days) after admission.(23)

Treatment

There are no specific recommendation for the SARS Cov 2 AP. The patient must be carefully monitored. There must be instituted the general supportive measures and fluid administration should be guided by patient's hemodynamic status. There must be a strict evaluation of the risk/benefit report in using the drug that might induce pancreatic lesions. The patients must be monitored after for diabetes (multifactorial, pancreas systemic inflammation, metabolic changes in organs, liver, adipose tissue, etc), pancreatic exocrine insufficiency, pancreatic induced local complication and chronic pancreatitis (22).

Conclusions

There are not enough data to prove that COVID 19 can cause AP.

Impact of COVID 19 on pancreas should rely on imaging preferably CT scan or magnetic resonance in patients with elevated pancreatic enzymes and COVID 19

There are no sufficient data to prove that COVID 19 can cause negative prognosis in time (Diabetes, pancreas exocrine insufficiency, chronic pancreatitis, etc).

There are necessary more prospective studies in pancreatic injury in COVID.

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